

AMENDMENT

Please amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents as follows.

IN THE CLAIMS

1. (Currently Amended) A retroviral vector comprising:
- (a) a 3' and 5' long terminal repeat (LTR); ~~the retroviral vector further comprising:~~
 - (a)(b) a functional splice donor site within the 5' LTR;
 - (b)(c) a functional splice acceptor site;
 - (c)(d) a first nucleotide sequence of interest ("NOI") (NOI) flanked upstream by the functional splice donor site and downstream by the functional splice acceptor site; and
 - (d)(e) a second NOI downstream of the functional splice acceptor site and upstream of the 3' LTR;

~~wherein the functional splice donor site is within the 5' LTR of the retroviral vector~~ whereby the first NOI is removed as a result of splicing.

2-4. (Cancelled)

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5. (Currently amended) The retroviral vector according to claim 1 wherein the second NOI, ~~or the~~ encodes a therapeutic or diagnostic expression product thereof, ~~is capable of providing a therapeutic agent or a diagnostic agent.~~

6. (Currently amended) The retroviral vector according to claim 1 wherein the first NOI, or the expression product thereof, comprises a selectable marker ~~[[,]]~~ or a viral element, ~~or a combination thereof.~~

7-8.

9. (Previously amended) The retroviral vector according to claim 1 wherein the functional splice donor site is from a virus.

10. (Previously amended) The retroviral vector according to claim 1 wherein the functional splice donor site is from an intron.

11. (Previously amended) The retroviral vector according to claim 10 wherein the intron is the small t-intron of SV40 virus.

12-13. (Cancelled)

14. (Currently amended) The retroviral vector according to claim 1 ~~wherein the functional splice acceptor site is upstream of~~ further comprising a multiple cloning site, such that one or more additional NOIs may be inserted wherein the functional splice acceptor site is located upstream of the multiple cloning site.

15. (Currently amended) The retroviral vector according to claim 1 wherein the functional splice acceptor site is from a nucleotide sequence coding for an immunological ~~molecule~~ protein.

16. (Currently amended) The retroviral vector according to claim 15 wherein the immunological ~~molecule~~ protein is an immunoglobulin.

17. (Previously amended) The retroviral vector according to claim 16 wherein the immunoglobulin is from an immunoglobulin heavy chain variable region.

18-20. (Cancelled)

21. (Currently amended) The retroviral vector according to claim 1 wherein the vector is a murine oncoretrovirus vector or a lentivirus ~~retroviral~~ vector.

22. (Currently amended) The retroviral vector according to claim 21 wherein the vector is a MMLV, MSV, MMTV, HIV-1 or EIAV retroviral vector.

23. (Cancelled)

24. (Currently amended) ~~The~~ A retroviral particle comprising the ~~obtained from a retroviral vector according to claim 1 wherein the retroviral particle comprises a retroviral vector comprising a functional splice donor site within its 5' long terminal repeat (LTR).~~

25-46. (Cancelled)

47. (Currently amended) A method of producing a retroviral vector comprising a functional splice donor site within its 5' long terminal repeat (LTR), the method comprising:

(a) providing a retroviral pro-vector comprising:

(i) ~~a 3' and 5' LTR;~~ the retroviral pro-vector comprising:

~~(i)~~ (ii) a functional splice donor site located within the 3' LTR;

~~(ii)~~ (iii) a functional splice acceptor site upstream of the splice donor site;

~~(iii)~~ (iv) a first nucleotide sequence of interest (NOI) upstream of the functional splice acceptor site and downstream of the 5' LTR, and

~~(iv)~~ (v) a second NOI downstream of the functional splice acceptor site and upstream of the 3' LTR;

- (b) packaging ~~the~~ the retroviral pro-vector in a packaging ~~host-primary~~ cell, thereby producing a viral particle; and
- (c) infecting a target ~~host-secondary~~ cell with the viral particle, wherein packaged pro-vector thereby causing reverse transcription of the retroviral pro-vector is reverse transcribed;

~~and production of the~~ thereby producing a retroviral vector comprising a functional splice donor site within its 5' LTR.

48. (Cancelled)

49. (Previously added) The method according to claim 47 wherein the first NOI is expressed in the ~~host-primary~~ packaging cell.

50. (Currently amended) The method according to claim ~~47~~ 49 wherein the first NOI is a selectable marker[[,]] or a viral element, or a combination thereof.

51. (Previously added) The method according to claim 50 wherein the viral element is a retroviral packaging signal, a retroviral envelope sequence, or a combination thereof.

52. (Cancelled)

53. (Previously added) The method according to claim 47 wherein the retroviral pro-vector is a murine oncoretrovirus pro-vector or a lentivirus retroviral pro-vector.

54. (Currently amended) The method according to claim 53 wherein the retroviral pro-vector is a MMLV, MSV, MMTV, HIV-1, or EIAV retroviral pro-vector.

55. (Currently amended) The method according to claim 47 wherein the retroviral pro-vector ~~further~~ comprises a heterologous transcriptional control sequence upstream of the functional splice donor site.

56. (Cancelled)

57. (Currently amended) A retroviral vector comprising:

(a) a 3' and 5' long terminal repeat (LTR); ~~the retroviral vector further comprising:~~

(a)(b) a functional splice donor site located within the 5' LTR;

(b)(c) a functional splice acceptor site located downstream of the functional splice donor site; and

(c)(d) an NOI downstream of the functional splice acceptor site and upstream of the 3' LTR;

whereby an intervening sequence between the functional splice donor site and the functional splice acceptor site is removed as a result of splicing~~wherein the functional splice donor site is within the 5' LTR of the retroviral vector.~~

58. (Currently amended) A retroviral particle comprising ~~obtained from~~ the retroviral vector according to claim 57 ~~wherein the retroviral particle comprises a retroviral vector comprising a functional splice donor site within its 5' long terminal repeat (LTR).~~

59. (Previously added) A retroviral vector comprising a functional splice donor site within its 5' LTR, wherein the retroviral vector is produced by the method of claim 47.

60. (New) The method according to claim 55, wherein the heterologous transcriptional control sequence is an internal promoter.

61. (New) The method according to claim 55, wherein the heterologous transcriptional control sequence is located in the 5' LTR.

62. (New) The method according to claim 55, wherein the heterologous transcriptional control sequence is located in the 3' LTR.

63. (New) The retroviral vector according to claim 57, wherein the intervening sequence comprises a viral element.

64. (New) The retroviral vector according to claim 63, wherein the viral element is a packaging signal.

65. (New) The retroviral vector according to claim 57, wherein the functional splice donor site is from a virus.

66. (New) The retroviral vector according to claim 57, wherein the functional splice donor site is from an intron.

67. (New) The retroviral vector according to claim 66, wherein the intron is the small t-intron of SV40 virus.

68. (New) The retroviral vector according to claim 57, further comprising a multiple cloning site, wherein the functional splice acceptor site is located upstream of the multiple cloning site.

69. (New) The retroviral vector according to claim 57, wherein the functional splice acceptor site is from a nucleotide sequence coding for an immunological protein.

70. (New) The retroviral vector according to claim 69, wherein the immunological protein is an immunoglobulin.

71. (New) The retroviral vector according to claim 70, wherein the immunoglobulin is from an immunoglobulin heavy chain variable region.

72. (New) The retroviral vector according to claim 57, wherein the vector is a murine oncoretrovirus vector or a lentivirus vector.

73. (New) The retroviral vector according to claim 72, wherein the vector is a MMLV, MSV, MMTV, HIV-1 or EIAV retroviral vector.

74. (New) A method of producing a retroviral vector comprising a functional splice donor site within its 5' LTR, the method comprising:

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- (a) providing a retroviral pro-vector comprising:
 - (i) a 3' and 5' LTR;
 - (ii) a functional splice donor site located within the 3' LTR;
 - (iii) a functional splice acceptor site;
 - (iv) an NOI downstream of the functional splice acceptor site and upstream of the 3' LTR;
 - (b) packaging the retroviral pro-vector in a packaging cell, thereby producing a viral particle; and
 - (c) infecting a target cell with the viral particle, wherein the retroviral pro-vector is reverse transcribed;

thereby producing a retroviral vector comprising a functional splice donor site within its 5' LTR.

75. (New) The method according to claim 74, wherein the retroviral pro-vector comprises a heterologous transcriptional control sequence upstream of the functional splice donor site.

76. (New) The method according to claim 75, wherein the heterologous transcriptional control sequence is an internal promoter.

77. (New) The method according to claim 75, wherein the heterologous transcriptional control sequence is located in the 5' LTR.

78. (New) The method according to claim 75, wherein the heterologous transcriptional control sequence is located in the 3' LTR.

79. (New) A retroviral vector comprising a functional splice donor site within its 5' LTR, wherein the retroviral vector is produced by the method of claim 74.
